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Proposed Re-evaluation Decision

# Propyzamide

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# Overview

## What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide propyzamide, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing propyzamide in Canada.

An evaluation of available scientific information found that products containing propyzamide do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of propyzamide uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing propyzamide registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for propyzamide and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of propyzamide.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

## What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Propyzamide, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in a 1994 RED and the *2002 Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED)*, the USEPA concluded that propyzamide was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED and TRED (Tolerance Reassessment Eligibility Decision) were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

## What Is Propyzamide?

Propyzamide is a herbicide that is used to control weeds in established ornamentals (i.e. iris, peony, ground covers [except *Vinca minor*] and coniferous trees and shrubs); ornamental nursery stock (container-grown coniferous trees and shrubs, in British Columbia only); established grass pastures or grass/legume (alfalfa, trefoil) pastures; alfalfa and trefoil grown for seed; apples, pears, lowbush blueberries, lettuce (direct seeded or transplanted) and strawberries (Maritimes and British Columbia only). Propyzamide is applied using a groundboom sprayer or a low-pressure handwand sprayer in greenhouses or outdoor areas by farm workers and professional applicators.

## Health Considerations

### Can Approved Uses of Propyzamide Affect Human Health?

**Propyzamide is unlikely to affect your health when used according to the revised label directions.**

People could be exposed to propyzamide by consuming food and water, by working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to

which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that propyzamide was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

**Maximum Residue Limits**

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Propyzamide is currently registered in Canada for use on alfalfa, apples, lowbush blueberries, lettuce, pears, strawberries and trefoil and could be used in other countries on crops that are imported into Canada. An MRL for propyzamide and its metabolites containing the 3,5-dichlorobenzoyl moiety and calculated as 3,5-dichloro-N-(1,1-dimethyl-2-propynyl)benzamide has been established for lettuce at 1 ppm. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

## Environmental Considerations

### What Happens When Propyzamide Is Introduced Into the Environment?

**Propyzamide is unlikely to affect non-target organisms when used according to the revised label directions.**

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) could be exposed to propyzamide in the environment. To assess the ecological effects of propyzamide, the USEPA used expected environmental concentrations (EECs) and maximum expected residues immediately after application and compared them to the lethal concentration to 50% ($LC_{50}$) for the various species.

The USEPA concluded that the reregistration of propyzamide was acceptable provided risk-reduction measures to further protect the environment were implemented. These

conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required. Furthermore, the PMRA will require terrestrial buffer zones for propyzamide to protect terrestrial plants from spray drift.

## Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of propyzamide, the PMRA is proposing further risk-reduction measures for product labels.

### Human Health

- Additional protective equipment to protect mixers/loaders/applicators
- A restricted-entry interval to protect workers re-entering treated sites
- A plantback interval to ensure minimal residues in rotational crops

### Environment

- Additional advisory label statements for the protection of surface water and groundwater sources
- Buffer zones to protect non-target, sensitive terrestrial habitats

## What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

## Next Steps

Before making a final re-evaluation decision on propyzamide, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

# Science Evaluation

## 1.0 Introduction

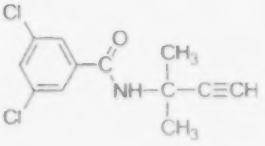
Propyzamide is a herbicide that acts by inhibiting plant cell division.

Following the re-evaluation announcement for propyzamide, the registrant of the technical grade active ingredient in Canada indicated its intention to provide continued support for all uses included on the labels of commercial and domestic end-use products currently registered in Canada.

The PMRA used recent assessments of propyzamide from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for propyzamide, dated 1994, and the USEPA Tolerance Reassessment and Eligibility Decision (TRED) (USEPA 2002) as well as other information on the regulatory status of propyzamide in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

## 2.0 The Technical Grade Active Ingredient, Its Properties and Uses

### 2.1 Identity of the Technical Grade Active Ingredient

| | |
|---|---|
| **Common name** | Propyzamide |
| **Function** | Herbicide |
| **Chemical family** | Benzamide |
| **Chemical name** | |
| 1 **International Union of Pure and Applied Chemistry (IUPAC)** | 3,5-dichloro-N-(1,1-dimethylpropynyl)benzamide |
| 2 **Chemical Abstracts Service (CAS)** | 3,5-dichloro-N-(1,1-dimethyl-2-propynyl)benzamide |
| **CAS Registry Number** | 23950-58-5 |
| **Molecular formula** | $C_{12}H_{11}Cl_2NO$ |
| **Structural formula** |  |
| **Molecular weight** | 256.1 |

| | |
|---|---|
| **Purity of the technical grade active ingredient** | 94.6% nominal (lower limit: 92%; upper limit: 98%) |
| **Registration Number** | 25594 |

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

## 2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

| Property | Result |
|---|---|
| Vapour pressure | 0.058 mPa at 25°C |
| Henry's law constant | $9.9 \times 10^{-4}$ Pa•m$^3$•mol$^{-1}$ |
| UV–visible spectrum | No absorption between 290–750 nm |
| Solubility in water | 15 ppm at 25°C |
| *n*-Octanol–water partition coefficient | Log $K_{ow}$ = 3.1–3.2 |

## 2.3 Comparison of Use Patterns in Canada and the United States

Propyzamide is a herbicide registered in Canada for the control of quackgrass, certain other perennial grasses such as orchardgrass and timothy, and most annual grasses, including wild oats and volunteer wheat. It acts by inhibiting plant cell division. It is used on established ornamentals (i.e. iris, peony, ground covers and coniferous trees and shrubs); ornamental nursery stock (container grown coniferous trees and shrubs; in British Columbia only); established grass pastures or grass/legume (alfalfa, trefoil) pastures; alfalfa and trefoil grown for seed; apples, pears, lowbush blueberries, lettuce (direct seeded or transplanted) and strawberries (Maritimes and British Columbia only). It is applied to the soil in the spring or fall. Propyzamide is applied once per year with a maximum application rate of 2.2 kg a.i./ha. The end-use product is formulated as a wettable powder packaged in water-soluble pouches and is applied to the soil using a groundboom sprayer or low-pressure hand sprayer in greenhouse or outdoor areas.

The American and Canadian use patterns were compared. Formulations, use sites (with the exception of use on strawberries), and maximum application rates and methods are encompassed by the American use pattern. Based on this comparison of use patterns, it was concluded that the USEPA RED for propyzamide is an adequate basis for the re-evaluation of Canadian uses of propyzamide.

All current uses are being supported by the registrant and were therefore considered in the re-evaluation of propyzamide. Appendix II lists all propyzamide products that are registered as of 14 February 2008 under the authority of the *Pest Control Products Act*.

## 3.0 Impact on Human Health and the Environment

In its 1994 RED, the USEPA concluded that the use of products containing propyzamide registered at the time of the RED publication would not pose unreasonable risks or adverse effects to humans or the environment and, therefore, are eligible for reregistration. After the RED, the USEPA published a TRED in 2002 that includes an aggregate risk assessment that met the *Food Quality Protection Act* requirements.

### 3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

In Canada, exposure to propyzamide may occur through consumption of food and water, through residential exposure, while working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

#### 3.1.1 Occupational Exposure and Risk Assessment

Where evidence of carcinogenicity is identified for the active ingredient, a cancer potency factor ($Q_1$*) is generated and used to estimate cancer risk. The product of the expected exposure and the $Q_1$* estimates the lifetime cancer risk as a probability. A lifetime cancer risk in the range of 1 in $10^{-5}$ to 1 in $10^{-6}$ in worker populations is generally considered acceptable. If the calculated risk is more than $1 \times 10^{-5}$, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to propyzamide when mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting or handling of treated crops.

##### 3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

It was determined that there were several exposure scenarios for occupational handlers of propyzamide. Specifically, exposure via the dermal route could occur during mixing/loading the wettable powder packaged in water-soluble bags or through applying sprays using either groundboom or hand-held equipment. Inhalation exposure was expected to be low and the occupational risk for this route of exposure was not assessed.

Among the scenarios assessed in the RED, the following exposure scenarios were considered relevant to the Canadian situation:

- mixing/loading wettable powder packaged in water-soluble bags and wearing a long-sleeved shirt, long pants, shoes, socks and gloves;
- applying sprays using groundboom equipment and wearing a long-sleeved shirt, long pants, shoes, socks and gloves;
- applying sprays using hand-held equipment and wearing a long-sleeved shirt, long pants, shoes, socks and gloves;
- mixing/loading/applying wettable powder packaged in water-soluble bags for groundboom application and wearing a long-sleeved shirt, long pants, shoes, socks and gloves;
- mixing/loading/applying wettable powder packaged in water-soluble bags for application with hand-held equipment and wearing a long-sleeved shirt, long pants, shoes, socks and gloves.

Handler exposure analyses were performed using chemical-specific dermal exposure data for mixing/loading wettable powder packaged in water-soluble bags and application using groundboom equipment. For the application by hand-held equipment, handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED). Estimated upper bound cancer risk was based on a maximum propyzamide application rate of 2.2 kg a.i./ha, 10 applications a year, a $Q_1$* of $1.54 \times 10^{-2}$ $(mg/kg\ bw/day)^{-1}$ and assuming 100% dermal absorption.

The USEPA reported acceptable cancer risk estimates ranging from $8 \times 10^{-6}$ to $2 \times 10^{-5}$. Based on this assessment and known toxicological concerns for propyzamide, including its classification as a Group B2 carcinogen, the USEPA required applicators and other handlers to wear coveralls over a short-sleeved shirt and short pants, chemical-resistant gloves, chemical-resistant footwear, socks, chemical-resistant headgear for overhead exposure and a chemical-resistant apron when cleaning equipment, mixing or loading.

In 2002, the USEPA published a TRED in which it conducted an assessment of aggregate risk for the purpose of reassessing tolerances. It was based on the same toxicological database as in the RED, with some revisions to the endpoint selection. As a result, short- and intermediate-term dermal and inhalation endpoints were selected and the value of the $Q_1$* was increased from $1.54 \times 10^{-2}$ $(mg/kg\ bw/day)^{-1}$ to $2.59 \times 10^{-2}$ $(mg/kg\ bw/day)^{-1}$.

The purpose of the 2002 assessment was tolerance reassessment and did not include revised estimates of risk from occupational activities. Although the potential occupational risk is not expected to be of concern, given the uncertainties in the USEPA assessment, additional data are required. This data includes a 21-day dermal toxicity study, a 28-day inhalation toxicity study, and a dermal absorption study in order to refine the risk assessment.

The PMRA is proposing that the following personal protective equipment be added to the end-use product label: coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, chemical-resistant footwear plus socks during mixing, loading and application. It is also proposing an indication on the label that a chemical-resistant apron should be worn when cleaning equipment, mixing or loading. A statement recommending that the product not be applied in a way that it will contact workers or other persons and that only handlers wearing personal protective equipment may be in the area during application is also proposed. The proposed label amendments are listed in Appendix IV.

#### 3.1.1.2 Postapplication Exposure and Risk

The postapplication occupational risk assessment considers exposures to workers entering treated sites. Based on the propyzamide use pattern, there is a potential for postapplication dermal exposure to foliar dislodgeable residues and soil residues. There may be less dermal exposure on agricultural sites if propyzamide is applied as a pre-emergence herbicide when the protected crop is still dormant. Postapplication inhalation exposure is expected to be minimal. Since data was unavailable, a quantitative postapplication risk assessment was not performed. However, a qualitative postapplication risk assessment was performed. Based on the carcinogenicity classification of propyzamide, a 24-hour restricted-entry interval (REI) was required for all uses, including ornamentals.

This was considered applicable to the Canadian situation, and the PMRA requires a 24-hour REI to further protect workers from postapplication exposure. The proposed label amendments are listed in Appendix IV.

### 3.1.2 Non-Occupational Exposure and Risk Assessment

#### 3.1.2.1 Residential Exposure

In Canada, the use of propyzamide on established ornamentals (i.e. iris, peony, ground covers [except *Vinca minor*] and coniferous trees and shrubs) may also include its use in residential areas such as public parks. This potential residential exposure scenario was not specifically assessed in the RED or the TRED. However, the TRED assessed scenarios of turf use with children/adults involved in low- to high-contact play/work activities or incidental ingestion (children). These assessments are considered worst-case scenarios because in Canada propyzamide is sprayed on the soil around established ornamentals and not on turf, and is applied only once in the fall. All USEPA-assessed scenarios were found acceptable except for the scenarios of incidental ingestion and direct turf contact involving children, which are not relevant to the ornamental use in Canada.

#### 3.1.2.2 Exposure From Food and Drinking Water

An acute dietary toxicological endpoint was not identified for exposure to propyzamide. On this basis, an acute dietary risk assessment was not conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the TRED, it is expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive segment of the population (see Appendix III).

When evidence of carcinogenicity is identified for the active ingredient, a cancer potency factor is generated and used to estimate cancer risk. The product of the expected exposure and the $Q_1$* estimates the lifetime cancer risk as a probability. A lifetime cancer risk below 1 in $10^{-6}$ usually does not indicate an unacceptable risk for the general population when exposure occurs through pesticide residues in or on food.

Refined Tier III chronic and cancer dietary risk assessments were conducted based on residue monitoring data for fruits and vegetables; tolerance levels for dried peas, endives, radicchio and cranberries; anticipated residues for meat, milk, poultry, eggs and percent crop treated data. Chronic exposure was estimated at <1% of the cPAD for the general population and all population groups, including infants and children, and a cancer risk estimate of $1.06 \times 10^{-7}$ was calculated for the general population. Based on this, the USEPA concluded that both chronic and cancer risk from food exposure were not considered to be of concern.

For groundwater, an upper bound estimated maximum chronic drinking water concentration of 3.0 ppb was calculated based on a Tier I groundwater screening model. This estimate was based on four applications of 2.24 kg a.i./ha per year. For surface water, 90$^{th}$ percentile average annual concentrations ranging from 1.5 to 6.4 ppb for use in the chronic exposure assessment and 36-year mean concentrations of 0.535 to 4.3 ppb for use in the cancer exposure assessment were calculated based on a Tier II surface water model. These estimates were based on application rates ranging from 1.68 to 4.48 kg a.i./ha with one application per year using different crop scenarios. Chronic and cancer risk assessments incorporating drinking water exposure estimates are discussed in the next section on aggregate risk (Section 3.1.2.3).

The current Canadian registered uses of propyzamide are encompassed by this assessment, with the exception of strawberries. Despite this minor difference in use pattern between the United States and Canada, this assessment is considered to be relevant to Canada based on the following.

- Less than 1% of the risk cup was used.
- A field trial conducted on strawberries in Canada at an application rate of ≤2.2 kg a.i./ha showed no detectable residues of propyzamide.

Based on the TRED, additional plantback intervals are proposed for the Canadian label. Appendix IV lists all proposed label amendments.

### 3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to propyzamide (i.e. from food, drinking water and residential exposures). Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short- and intermediate-term aggregate risk assessments examine contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

Acute aggregate risk was not estimated as no acute toxicological endpoints of concern were identified for propyzamide.

Short-term aggregate risk combined estimates of exposures from food, drinking water and postapplication residential exposure. Drinking water levels of concern (DWLOCs) were calculated by subtracting the average food exposure plus residential exposure from the maximum exposure. These DWLOCs were then compared to the EECs for drinking water. The groundwater EEC of 3.0 ppb and the surface water EECs of 1.5 to 6.4 ppb did not exceed the short-term DWLOC of 560 (highest exposed adult population group). Short-term postapplication dermal/incidental oral exposure of children to propyzamide on lawns resulted in risk estimates exceeding levels of concern. However, since the registrant in the United States is no longer supporting this use, short-term aggregate risk to children was no longer a concern.

The assessment of chronic aggregate risk combined exposure from food and drinking water. DWLOCs were calculated by subtracting the chronic dietary food exposure from the cPAD to obtain acceptable chronic exposure levels to propyzamide in drinking water. These DWLOCs were then compared to the EECs for drinking water. The chronic groundwater EEC of 3.0 ppb and the chronic surface water EECs of 1.5 to 6.4 ppb did not exceed the chronic DWLOCs of 1050 (general population), 900 (females 13–50 years old), and 300 (infants and children 1–6 years old). The USEPA considered the estimated combined chronic exposure to propyzamide from food and drinking water to be below its level of concern.

The assessment of cancer aggregate risk combined exposure from food and drinking water. The cancer groundwater EEC of 3.0 ppb and the cancer surface water EECs of 0.535 to 4.35 ppb exceeded the cancer DWLOC of 1.2 ppb. However, the USEPA concluded that the cancer risk assessment was conservative because of the following assumptions:

- maximum label rates (typical rates being 25–50% less);
- percent crop area of 87% (likely to be an overestimation);
- a 2 to 3 times uncertainty factor for soil and water half-lives used in drinking water (from surface water) modelling because data from only one soil type was available.

In Canada, propyzamide is applied once per year at a maximum application rate of 2.2 kg a.i./ha. Therefore, the USEPA drinking water estimates are considered to be an overestimate of the Canadian situation (i.e. groundwater EEC was based on four applications of 2.24 kg a.i./ha and the high-end surface water estimates were based on a rate of 4.48 kg a.i./ha). Furthermore, there

is no turf use registered in Canada. Overall, the Canadian potential aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of propyzamide in Canada and no further mitigation is required.

### 3.1.3 Cumulative Effects

The USEPA has not determined whether propyzamide has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that propyzamide does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

## 3.2 Environment

### 3.2.1 Environmental Risk Assessment

Based on laboratory data, the USEPA determined that propyzamide was stable to hydrolysis and photolysis both in water and on soil. Propyzamide was also found to be very persistent in soil under aerobic conditions (half-life of 392 days) and even more persistent under anaerobic conditions. Propyzamide was found to have a relatively low vapour pressure and to be relatively mobile in soil, with leaching appearing to be the major route of dissipation. Based on this, the USEPA concluded that propyzamide would be expected to be relatively persistent and mobile in the field.

To assess the ecological effects of propyzamide, the USEPA calculated EECs for aquatic scenarios and maximum expected residues immediately after application for terrestrial scenarios, and compared these values to the relevant $LC_{50}$.

The USEPA determined that, on an acute basis, propyzamide was practically non-toxic to birds and mammals. Maximum expected residues immediately after application did not exceed the avian acute $LC_{50}$ or the mammalian acute $LC_{50}$. Although propyzamide is persistent, chronic exposure to birds and mammals was not expected because propyzamide is only applied once per season, it is soluble in water and would wash off avian food items, and it is practically non-toxic to birds.

Propyzamide was found to be slightly toxic to freshwater fish and moderately toxic to freshwater invertebrates. The aquatic EEC did not exceed the acute $LC_{50}$ for fish or the acute $LC_{50}$ for invertebrates. However, based on the moderate acute toxicity to invertebrates (i.e. *Daphnia magna*) and the potential persistence and mobility of propyzamide in the aquatic environment, an aquatic invertebrate life cycle study was required to assess potential chronic risk. A mollusc and shrimp study were also required in order to establish toxicity to estuarine and marine invertebrates.

Propyzamide was found to be toxic to green algae. However, the aquatic plant data were found to be insufficient (i.e. only one supplemental study on green algae available) and additional data was required. It was also reported that non-target terrestrial plants may be adversely affected by runoff and spray drift.

The American use pattern for propyzamide encompasses the Canadian use pattern, and the USEPA conclusions are relevant to Canada. As in the United States, the PMRA requires that additional advisory label statements for the protection of surface water and groundwater sources be added to the label.

The PMRA also requires terrestrial buffer zones for formulations of propyzamide to protect terrestrial plants from spray drift during propyzamide application. Aquatic buffer zones are currently not required based on the green algae (*Selenastrum capricornutum*) toxicity endpoint from the RED. In order for the PMRA to confirm aquatic buffer zone calculations to adequately protect aquatic habitats, additional data on aquatic plants and a chronic aquatic invertebrate study (due to potential persistence and mobility of propyzamide) are required.

Data requirements are detailed in Appendix I. Proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are listed in Appendix V.

### 3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal TSMP, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal TSMP and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of propyzamide. The PMRA has reached the following conclusions.

- Propyzamide is not bioaccumulative; the *n*-octanol–water partition coefficient (log $K_{ow}$) is 3.1–3.2, which is below the TSMP Track 1 cut-off criterion of ≥5.0. Propyzamide was found to be persistent; aerobic soil half-lives are greater than 90 days, and even more persistent under anaerobic conditions with an estimated anaerobic soil half-life greater than 13 months. Propyzamide does not meet all Track 1 criteria, and thus it is not a candidate for Track 1 classification.

- Based on a review of the available chemistry information (see Section 2.1), the technical product is not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

## 4.0 Proposed Re-evaluation Decision

The PMRA has determined that propyzamide is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The label of the Canadian end-use product must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

## 5.0 Data Required as a Condition of Continued Registration

Toxicity data for short-term dermal and inhalation exposure and a dermal absorption study are required to make a final determination of occupational risk. Aquatic buffer zones of zero metres were calculated based on limited ecotoxicity data from the RED. In order for the PMRA to confirm aquatic buffer zone calculations to adequately protect aquatic habitats, additional data on aquatic plants and a chronic aquatic invertebrate study are required. Appendix I lists all data requirements.

## 6.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for propyzamide is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

## List of Abbreviations

| | |
|---|---|
| µg | microgram |
| ADI | acceptable daily intake |
| a.i. | active ingredient |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| cm | centimetre(s) |
| cPAD | chronic population adjusted dose |
| cRfD | chronic reference dose |
| DACO | data code |
| DWLOC | drinking water level of comparison |
| $EC_{25}$ | effect concentration 25% |
| $EC_{50}$ | effect concentration 50% |
| EEC | expected environmental concentration |
| FQPA | *Food Quality Protection Act* |
| g | gram(s) |
| ha | hectare(s) |
| kg | kilogram(s) |
| $K_{ow}$ | *n*-octanol–water partition coefficient |
| L | litre(s) |
| $LC_{50}$ | lethal concentration to 50% |
| LOC | level of concern |
| m | metre(s) |
| $m^3$ | metre(s) cubed |
| mg | milligram(s) |
| MOE | margin of exposure |
| MRL | maximum residue limit |
| nm | nanometre(s) |
| NOAEL | no observed adverse effect level |
| PMRA | Pest Management Regulatory Agency |
| ppb | parts per billion |
| ppm | parts per million |
| $Q_1^*$ | cancer potency factor |
| RED | Reregistration Eligibility Decision |
| REI | restricted-entry interval |
| RQ | risk quotient |
| SF | safety factor |
| TRED | Tolerance Reassessment Eligibility Decision |
| TSMP | Toxic Substances Management Policy |
| UF | uncertainty factor |
| USEPA | United States Environmental Protection Agency |
| UV | ultraviolet |

## Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrant of this active ingredient must provide these data within the timeline specified in the decision letter that the PMRA will send to the registrant.

1) For the PMRA to confirm occupational risk, the following data are required:

- DACO 4.3.5 Short-term Dermal (21/28-day)
- DACO 4.3.7 Short-term Inhalation (21/28-day)
- DACO 5.8 Dermal absorption study (in vivo)

2) In order for the PMRA to confirm aquatic buffer zones to adequately protect sensitive aquatic habitats, the following data are required:

- DACO 9.3.3 Non-target Freshwater Invertebrate; *Daphnia sp.* Chronic (Life-Cycle)
- DACO 9.8.2 Fresh Water Algae (*Skeletonema costatum*, *Anabaena flos-aquae*, and a freshwater diatom)
- DACO 9.8.5 Non-target Plants - Aquatic Vascular Plants (*Lemna gibba*)

# Appendix II Registered Products Containing Propyzamide as of 14 February 2008

| Registration Number | Marketing Class | Registrant | Product Name | Formulation Type | Guarantee (%) |
|---|---|---|---|---|---|
| 25594 | Technical | Dow Agrosciences Canada Inc. | Kerb Technical Herbicide | Solid | 94.6 |
| 25595 | Commercial | Dow Agrosciences Canada Inc. | Kerb 50 WSP Selective Herbicide | Wettable powder | 50 |

# Appendix III Toxicological Endpoints for Propyzamide Health Risk Assessments

| Exposure Scenario (route and period of exposure) | Dose (mg/kg bw/day) | Study | Target UF/SF or MOE or Q* [a] |
|---|---|---|---|
| Chronic dietary—all populations | NOAEL = 8.46 | Combined chronic toxicity/carcinogenicity study in rat | UF = 100<br>FQPA SF = 3 |
| | cRfD = 0.08 mg/kg bw/day<br>cPAD = 0.027 mg/kg bw/day (i.e. cRfD/FQPA SF) | | |
| Short-term oral—residential | NOAEL = 8.46 | Developmental toxicity study in rabbit | UF = 100<br>FQPA SF = 3 |
| Intermediate-term oral—residential | NOAEL = 8.46 | Combined chronic toxicity/carcinogenicity study in rat | UF = 100<br>FQPA SF = 3 |
| Short-term dermal—occupational/residential | NOAEL = 8.46<br><br>Dermal absorption rate = 100% | Developmental toxicity study in rabbit | UF = 100<br>FQPA SF = 3 |
| Intermediate-term dermal—occupational/residential | NOAEL = 8.46<br>Dermal absorption rate = 100% | Combined chronic toxicity/carcinogenicity study in rat | UF = 100<br>FQPA SF = 3 |
| Short-term inhalation—occupational/residential | NOAEL = 8.46<br>Inhalation absorption rate = 100% | Developmental toxicity study in rabbit | UF = 100<br>FQPA SF = 3 |
| Intermediate-term inhalation—occupational/residential | NOAEL = 8.46<br>Inhalation absorption rate = 100% | Combined chronic toxicity/carcinogenicity study in rat | UF = 100<br>FQPA SF = 3 |
| Cancer (oral, dermal, inhalation) | Group B2 - "Probable human carcinogen" | Combined chronic toxicity/carcinogenicity study in rat | $Q_1^* = 2.59 \times 10^{-2}$ $(mg/kg/day)^{-1}$ |

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments. MOE refers to desired margin of exposure for occupational or residential assessments. $Q_1^*$ refers to cancer potency factor.

# Appendix IV Label Amendments for Products Containing Propyzamide

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following statements must be included in the **PRECAUTIONS** section.

Wear coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, chemical-resistant footwear plus socks during mixing, loading and application. In addition, wear a chemical-resistant apron when cleaning equipment, mixing or loading.

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 24 hours.

It is recommended that this product not be applied in a way that will contact workers or other persons, either directly or through drift. Only handlers wearing personal protective equipment may be in the area during application.

II) The following statements must be included in the **DIRECTIONS FOR USE** section.

Rotational crops: Observe a plantback interval of 30 days for leafy vegetables (except *Brassica* vegetables), 90 days for root and tuber vegetables and 360 days for all other crops.

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

DO NOT apply by air.

**Buffer zones:**

Use of the following spray methods or equipment DO NOT require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands).

| Method of Application | Crop | Buffer Zones (metres) Required for the Protection of: |
|---|---|---|
| | | Terrestrial habitat |
| Field sprayer* | Established grass pastures, established grass/legume (alfalfa, trefoil) pastures, alfalfa grown for seed, trefoil grown for seed, strawberries, lettuce, established ornamentals | 5 |
| | Lowbush blueberries, apples, pears | 10 |

* For field sprayer application, buffer zones can be reduced with the use of drift-reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

III) The following statements must be included in the **ENVIRONMENTAL HAZARDS** section.

TOXIC to non-target terrestrial plants. Observe buffer zones specified under **DIRECTIONS FOR USE**.

DO NOT apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), estuarine/marine habitats.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

DO NOT allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters.

The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

# Appendix V Inputs to Buffer Zone Models

| Ground Use Data (from Canadian labels) | | | | |
|---|---|---|---|---|
| **Crop** | **Formulation Type** | **Method of Application** | **Number of Applications** | **Maximum Application Rate (g a.i./ha)** |
| Alfalfa, trefoil, pastures | Wettable powder | Field sprayer | 1 | 1625 |
| Ornamentals | Wettable powder | Field sprayer | 1 | 1500 |
| Strawberries, lettuce | Wettable powder | Field sprayer | 1 | 1125 |
| Blueberries, apples, pears | Wettable powder | Field sprayer | 1 | 2250 |

| Model Input Data for Aquatic Buffer Zones (from 1994 RED) | | |
|---|---|---|
| Half-life for aquatic buffer zones | Not available | Considered stable |
| Most sensitive amphibian species | Rainbow trout (used as surrogate data) | 1/10 $LC_{50}$ = 7.2 ppm |
| Most sensitive freshwater species | *Selenastrum capricornutum* | ½ $EC_{50}$ = 0.38 ppm |
| Most sensitive estuarine/marine species | *Selenastrum capricornutum* (used as surrogate data) | ½ $EC_{50}$ = 0.38 ppm |

| Model Input Data for Terrestrial Buffer Zones (from 1994 RED) | | |
|---|---|---|
| Half-life for terrestrial buffer zones | Soil degradation half-life | 392 days |
| Most sensitive terrestrial plant species | Ryegrass - seedling emergence | $EC_{25}$ = 7.5 g a.i./ha |

# References

## A. List of Studies/Information Submitted by Registrant


PMRA 1564292 Technical Chemistry for KRB-DCE-1. Kerb 50-W Active Ingredient Specifications, Analysis of Kerb Wet Cake,Test Method 1-4, 2-5, and 203-2., DACO: 2.99

PMRA 1564367 Technical Chemistry file KRB-DCE-1., DACO: 2.1, 2.10, 2.11.1, 2.12.2, 2.13.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9

PMRA 1564287 Technical Chemistry for KRB-DCE-1. Response to Outstanding Product Chemistry Requirements, Appearance Samples, Propyzamide (Pure) Spectral Data, Aqueous Solubility Conducted in Germany, Solubility in Organic Solvents., DACO: 2.14

PMRA 1564275 1994, Technical Chemistry for KRB-DCE-1. Submitted for the purpose of verifying the change in the production site of Kerb